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PROSTHETIC STRUCTURES FROM MICRO-CRYSTALLINE COLLAGEN

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No Drawing. Filed Sept. 1, 1967, Ser. No. 664,955

Int. Cl. A61f 1/00

U.S. Cl. 3—1

15 Claims

ABSTRACT OF THE DISCLOSURE

Artificial ivory and bone-like structures formed from a homogeneous mixture of a water-insoluble, microcrystalline ionizable salt of collagen, calcium phosphate and water. Fibers may be included to improve strengths, other ions may be included to increase hardness and collagen cross-linking agents may be included to improve moisture and water-resistance.

This invention relates to a new composition of matter, particularly well suited for prosthetic devices, and to a process for manufacturing the same.

The supporting skeleton of vertebras consists of cartilage and bone. In the embryonic stages, cartilage forms this supporting skeleton and most of the cartilage is replaced in the adult by bone. Cartilage persists in adults at bone joints and in other locations such as the ear, nose, etc. The principal organic constituent of cartilage and bone tissue is collagen and the principal inorganic component in cartilage and bone tissue is calcium phosphate complexes or compounds such as, for example, hydroxyapatite. The chief inorganic constituents are calcium, magnesium, phosphate radicals, carbonate radicals, the fluoride radical and water, the compounds being of varying compositions generally belonging to the apatite group. Other inorganic ions are generally present in trace amounts and other organic matter is also present. The other elements found in minor and trace amounts in bone tissue are aluminum, barium, boron, chlorine, copper, iron, lead, manganese, potassium, sodium, strontium and tin while arsenic, bismuth, lithium, molybdenum, nickel, selenium, silicon, silver and zinc have been detected spectrographically. In general, the differences in hardness and rigidity between cartilage and bone tissue are due to the differences in composition such as differences in the ratios of collagen to the inorganic calcium phosphate compounds and the presence of other radicals as well as the morphological structure.

The bone tissue consists of bundles of collagenous fibers in an amorphous cement material which is probably a protein-polysaccharide complex impregnated with the calcium phosphate complexes or compounds. Sulfur is also included and appears to be present as ester sulfate associated with the polysaccharides. Differences in hardness and other characteristics of the different bone tissues and parts of bone are believed to be due to variations in amounts of calcium carbonate and other constituents such as magnesium, fluorine, carbonate, etc. absorbed on the surface of the hydroxyapatite crystals or the fluoride and carbonate radical may replace the hydroxy radical. Regardless of the precise manner in which these additional substances are associated with the calcium phosphate compounds, these substances appear to alter the crystal lattices of the phosphate compounds. Differences in physical characteristics are also influenced by the morphology of the specific or individual bone tissue. Roughly, the ratio of the collagenous material to the inorganic material in the human bone is slightly less than 1:3, varying from about 1:2.65 to about 1:2.89 in the human femur,

based on the weight of dry defatted bone. The foregoing is obviously an oversimplification of the structure and composition of bone tissue which in fact is a most complex structure varying in precise composition with age, individual and species of mammals.

The precise method by which this class of tissue is formed is not known. Physico-chemical theories have been advanced in an attempt to explain the formation of dental calculus and it is possible that bone tissue might be formed in a somewhat similar manner. According to this theory, saliva is considered to be a colloidal solution of proteins which is more or less saturated with calcium and phosphate ions. Surface tension is believed to cause the proteins to concentrate at the surface of the saliva thus reducing the viscosity of the liquid and causing a settling out of inorganic salts which deposit on the teeth surfaces.

Thus far, cartilage and bone tissue has not been formed or duplicated synthetically. In bone surgery, a variety of materials has been used including bone, bone derivatives and synthetic substitutes. Bone from which certain constituents such as minerals, proteins, lipids and water have been removed is generally classed as bone derivative. Synthetic substitutes include metals, certain synthetic polymers, calcium sulfate and hydroxyapatite.

The chemistry of sparingly soluble phosphate salts or specifically the system $\text{Ca}-\text{P}_2\text{O}_5-2\text{H}_2\text{O}$ and the precise chemistry and structure of the calcium phosphate compounds occurring in natural cartilage and bone tissue are extremely complex. Accordingly, the term "calcium phosphate" is used herein and in the claims to include dicalcium phosphate, tricalcium phosphate, octacalcium phosphate, hydroxyapatite, carbonate-apatite, chlorapatite, fluorapatite and mixtures thereof.

One of the principal purposes of this invention is to provide a new composition of matter which more closely resembles cartilage and bone tissue than the prior synthetic substitutes and to provide a method of forming such composition of matter.

Another purpose of the present invention is to provide prosthetic devices by a synthetic method which more closely resemble cartilage and bone than the synthetic substitutes now available.

The present invention contemplates forming a new composition of matter comprising a water-insoluble microcrystalline partial salt of collagen and calcium phosphate by forming an aqueous colloidal gel or dispersion of the microcrystalline collagen salt and a calcium phosphate in a mesoamorphous state and altering the mesoamorphous structure. Other desired ions and the so-called trace elements and radicals may be included in the dispersion such as, for example, fluorine, carbonate, etc. so as to form fluoroapatite and carbonate-calcium phosphate compounds such as, for example, the hydroxyapatite-carbonate compounds present in some bone tissues. The relative hardness, flexibility, plasticity and rigidity is, in part, dependent upon the relative proportions of the organic and inorganic constituents and the structural morphology. The ratio of the microcrystalline collagen salt to the calcium phosphate and other inorganic constituents may vary from about 1:20 to about 1:0.01. As is apparent, the higher the inorganic content, the more rigid and dense the product. Hardness and density may also be varied by the alteration of the mesoamorphous state of the calcium phosphate and by the proportion of the carbonate and/or fluoride radicals present.

In the mammals, cartilage and bone must withstand one or more of several forces such as compression, bending, twisting and impact forces. The resistance to some of these forces and certain of the physical strength characteristics of the products of this invention may be altered